DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

This is an untilled letter from FDA -

Food and Drug Administration
Rockville MD 20857

RECEIVED

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LAW DEPARTMENT

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Rick suggested everyone have a copy so we understand the level of scrutiny we are under.) — Monica

Monica Krieger, Ph.D.
CellPro, Incorporated
22215 26th Avenue SE
Bothell, Washington 98021

Dear Dr. Krieger:

We are in receipt of a holiday greeting card that was disseminated by your company during the month of December, 1996. A copy is enclosed. Appearing on the back cover of the card is information about the artist which contains facts and efficacy claims related to a new indication for use of your CEPRATE® SC Stem Cell Concentration System for which a supplemental application has not been approved. As described in the conditions for approval of this device, no advertisement or other descriptive printed material issued by you or a distributor shall recommend or imply that the device may be utilized for uses that are not included in the FDA approved labeling.

The CEPRATE® SC Stem Cell Concentration System, manufactured by CellPro, Inc., is considered to be a device within the meaning of section 201(h) of the Federal Food Drug and Cosmetic Act (the Act). This device was approved for sale and distribution as a restricted device under the Premarket Approval (PMA) process described in section 515(d)(1)(B)(ii) of the Act for the following indication [Reference PMA Number BP940001]:

"...for the processing of autologous bone marrow to obtain a CD34+ cell enriched population which is intended for hematopoietic support after myeloablative chemotherapy."

The specific areas of concern related to the promotion of this device are noted below.

a. In your "about the artist" profile, a brief discussion regarding the use of the CEPRATE system in allogeneic stem cell transplants appears in the second paragraph.

> The evaluation of stem cell transplants from allogeneic donors (e.g. use of stem cells from parents who are half-matched at tissue type antigens) is still experimental. Thus far, the Center for Biologics Evaluation and Research (CBER) has not received data from you that would render conclusive evidence to base your claim for use of the device in allogeneic transplants thereby expanding the donor pool and providing many more children with curative treatment of high risk leukemia. The new indication for use of this device described above may not be promoted until a PMA Supplement has been submitted and approved.

b. In the third paragraph of the "about the artist" profile, the following claim is made: "Selecting stem cells reduces the chances of severe graft-versus-host disease that would otherwise occur if a child were to receive a half-matched bone marrow transplant from a parent"

> CBER has not received a supplement to your PMA providing the clinical data that would provide the evidence needed to support this claim. In the absence of this information, one cannot conclude that CEPRATE®-selected (T- cell depleted) allogeneic transplants will prevent graft-versus-host disease or otherwise confer a benefit to the patient.

The above mentioned misrepresentations or like misrepresentations about the CellPro CEPRATE® device misbrand your product under Section 502(o) in that you have failed to comply with Section 515 of the Act. Section 515 of the Act requires that you file a PMA Supplement in accordance with the provisions described in 21 CFR Part 814.39. This regulation requires that an applicant submit a PMA Supplement before making a change affecting the safety or effectiveness of the device for which the applicant has an approved PMA. We have determined the aforementioned claims regarding the CEPRATE® system affect both the safety and

efficacy of this device and, therefore, require the submission of a supplement that would provide the definitive evidence to support such claims.

In addition, as a restricted device, you are further misbranding your device under Section 502(q)(1) of the Act, by including uses and claims in your advertising for this device that are regarded to be false and misleading.

It is your responsibility to ensure that the violations noted in this letter that may appear in other advertising or promotional materials are also corrected. You should take prompt action to correct the violations noted and assure compliance with the applicable regulations.

Please respond to this staff, in writing, within 15 days of the receipt of this letter. Your response should include the steps you plan on taking to remedy the above noted observations. Please send your response to the attention of:

Ms. Toni M. Stifano
Center for Biologics Evaluation and Research
Advertising and Promotional Labeling Staff, HFM-202
1401 Rockville Pike
Rockville, MD 20852-1448

Sincerely yours,

William V. Purvis
Director, Advertising and Promotional
Labeling Staff
Center for Biologics Evaluation
and Research

Enclosure

About the Artist

Thomas Green, our holiday guest artist, celebrated his sixth birthday on September 19th, and does just about all the things a healthy six-year-old does. But when he was six years old, Thomas was diagnosed with acute myelocytic leukemia (AML). He received chemotherapy treatments, spent weeks in the hospital, and had problems with fevers and low blood counts. Although his AML initially responded to the chemotherapy, it relapsed just a few months later and required more intensive antileukemia drug treatments. Thomas was again on the list for treatment of complications like bloodstream infections, and he endured numerous bone marrow tests and spinal taps in the clinic and in the hospital.

After further chemotherapy, his leukemia went into a second remission. Thomas's doctors knew that the best chance to cure his AML was with a bone marrow transplant. But Thomas's sister was not a tissue type (HLA) match, and there was not time to find a suitable matched unrelated bone marrow donor. Faced with this dilemma, his family and doctors searched for other treatment options. They found out that physician investigators at the Winship Cancer Institute Transplant Program at Emory University and Egleston Children's Hospital in Atlanta were evaluating stem cell transplants from parents to children using the stem cell selection technology pioneered by CellPro, Incorporated. Using parents, who are half-matched at the tissue type antigens, as stem cell donors for their children greatly expands the donor pool and could provide many more children with curative treatment of high-risk leukemia.

A medical device developed by CellPro, called the CEPRATE® Stem Cell Concentration System, allowed the Emory physicians to select and purify the stem cells from Thomas's mother's bone marrow and peripheral blood cells. Selecting stem cells reduces the chances of severe graft-versus-host disease that would otherwise occur if a child were to receive a half matched bone marrow transplant from a parent.

Under the direction of Andrew M. Yeager, M.D., Professor of Pediatrics and Medicine at Emory University, Thomas received a stem cell transplant from his mother, Nancy Green, in January 1995. Within two weeks after the stem cell transplant, Thomas's blood counts were returning to normal and there was no evidence of AML. Now almost two years after transplant, Thomas is off all medications, has normal blood counts, has no graft-versus-host disease, and most importantly, has no AML. He's back leading a busy normal life, baseball, school, little league, and an avid interest in outer space. He even found a bit of spare time to provide the artwork for this holiday greeting from CellPro!